



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
Address : COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/652, 978	02/08/91	BUHR	C 4610-0027
18N1/0322			
KUNZ, G. EXAMINER			
NANCY JOYCE GRACEY. MORRISON & FOERSTER 755 PAGE MILL ROAD PALO ALTO, CA 94304-1018		ART UNIT	PAPER NUMBER
		1803	21

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

This application has been examined       Responsive to communication filed on 12/15/93       This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1.  Notice of References Cited by Examiner, PTO-892.
2.  Notice re Patent Drawing, PTO-948.
3.  Notice of Art Cited by Applicant, PTO-1449.
4.  Notice of Informal Patent Application, Form PTO-152.
5.  Information on How to Effect Drawing Changes, PTO-1474.
6.

Part II SUMMARY OF ACTION

1.  Claims 7-18, 20, 22, and 27-46 are pending in the application.

Of the above, claims \_\_\_\_\_ are withdrawn from consideration.

2.  Claims \_\_\_\_\_ have been cancelled.

3.  Claims \_\_\_\_\_ are allowed.

4.  Claims 7-18, 20, 22, and 27-46 are rejected.

5.  Claims \_\_\_\_\_ are objected to.

6.  Claims \_\_\_\_\_ are subject to restriction or election requirement.

7.  This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8.  Formal drawings are required in response to this Office action.

9.  The corrected or substitute drawings have been received on \_\_\_\_\_: Under 37 C.F.R. 1.84 these drawings are  acceptable.  not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10.  The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_ has (have) been  approved by the examiner.  disapproved by the examiner (see explanation).

11.  The proposed drawing correction, filed on \_\_\_\_\_, has been  approved.  disapproved (see explanation).

12.  Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has  been received  not been received  been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_

13.  Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14.  Other

07/652, 978  
PTOL-326 (Rev. 9-89)

EXAMINER'S ACTION

Applicant's Amendment B filed December 15, 1993 has been received and entered into the record.

Claims 7 - 18, 22, and 27 - 46 are pending in the case.

Any 35 USC statutes referenced but not cited in full in this Office action can be found in the first Office action on the merits mailed November 25, 1992 (Paper No. 11).

Claims 7 - 18, 22, and 27 - 46 are rejected under 35 USC 103 as being obvious over Martin et al., Robbins et al., Ranganathan or Watanabe et al. or Webb et al. or Tisdale in view of Padyukova et al. (Tetrahedron Letters 28: 3623 - 3626, 1987) and Barton et al. (Tetrahedron Letters, 30: 4969 - 4972, 1989). As already pointed out in the Office action mailed August 9, 1993 (Paper No. 17), the first six references above disclosure one or more of the claimed nucleoside analogs without the 5'-phosphonate moiety. However, Padyukova et al. and Barton et al. articles disclose the methylene isostere of the 5'-O-monophosphate nucleosides. The Padyukova et al. article teaches that such nucleoside phosphonate derivatives can be used for the synthesis of oligonucleotides (page 3625, paragraph 3). Furthermore, the Barton et al. article discloses AZT 5'-CH<sub>2</sub>-phosphonate (compound 13) to be a highly promising candidate as an anti-HIV drug (page 4971, last sentence).

Consequently, the 5'-CH<sub>2</sub>-phosphonate derivatives of nucleosides would have been obvious to the person of ordinary skill in the art at the time of the invention wanting to in-

corporate said nucleotide derivative into oligonucleotides or wanting to develop another nucleoside derivative with comparable or better antiviral activity to the unmodified nucleoside analog. Thus, the invention is prima facie in the absence of clear and convincing evidence to the contrary.

The applicant has traversed this obviousness rejection on the basis that there is no clear motivation for combining the references apart from the reasons found in the specification. This argument has been fully considered but is not deemed persuasive. The Padyudova et al. reference teaches one motivation for preparing the 5'-phosphonate derivatives of free nucleosides and/or nucleoside analogs: to prepare oligonucleotides with them. The Barton et al. reference teaches another motivation: to prepare another derivative that should have comparable or better properties than the free nucleoside analog itself.

The rejections of under 35 USC 112, first and second paragraphs, in the previous Office action mailed August 9, 1993 (Paper No. 17) are withdrawn in view of the amendments of claims 7, 10, 14, 20, and 38 - 42.

No claim is allowed.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mail 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier

Serial No. 07/652,978  
Art Unit 1803

-4-

communications from the examiner should be directed to Examiner Kunz whose telephone number is (703) 308-4623.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*Johnnie R. Brown*  
JOHNNIE R. BROWN  
SUPERVISORY PATENT EXAMINER  
ART UNIT 183

Gary L. Kunz, Ph.D.  
March 20, 1994